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Supplemental Information

Encoding of Target Detection during Visual Search by Single Neurons in the Human Brain

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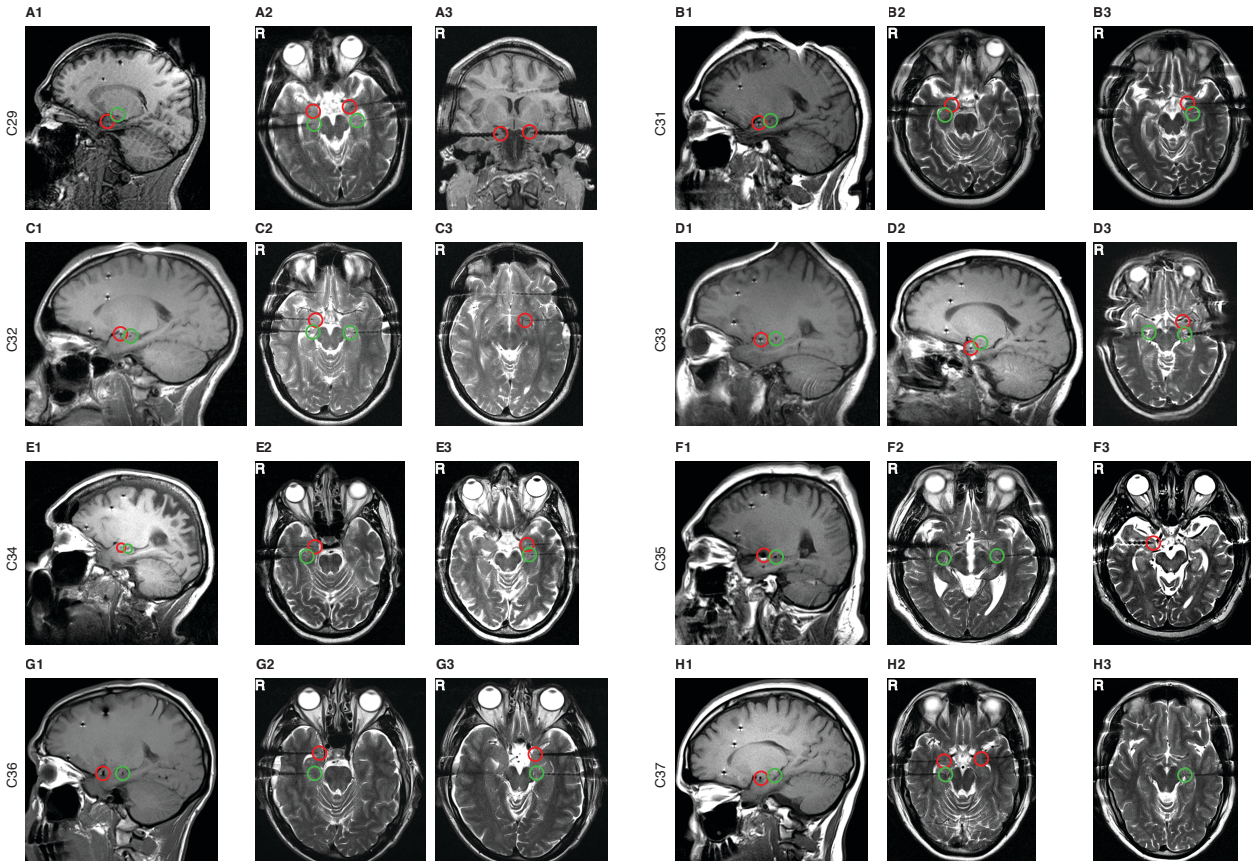

Figure S1. Electrode localization with structural MRIs, Related to Figure 2. Recording sites were verified for each patient with post-implantation MRIs. **(A1, B1, C1, D1, D2, E1, F1, G1, H1)** Sagittal T1 FLAIR image (0.957 × 0.957 mm in-plane, 5 mm thick, TR = 449 ms, TE = 10 ms, flip angle = 90°). **(A1, C1, D2, F1, H1)** Right side of the brain. **(B1, D1, E1, G1)** Left side of the brain. **(A2, B2, B3, C2, C3, D3, E2, E3, F2, F3, G2, G3, H2, H3)** Axial T2 image (0.9375 × 0.9375 mm in-plane, 2 mm thick, TR = 2500 ms, TE = 147 ms, flip angle = 180°). **(A3)** Coronal T1 image (0.859 × 0.859 mm in-plane, 1.2 mm thick, TR = 1400 ms, TE = 4.4 ms, flip angle = 15°). Red and green circles denote estimated recording regions of the amygdala and hippocampus, respectively. R: right.

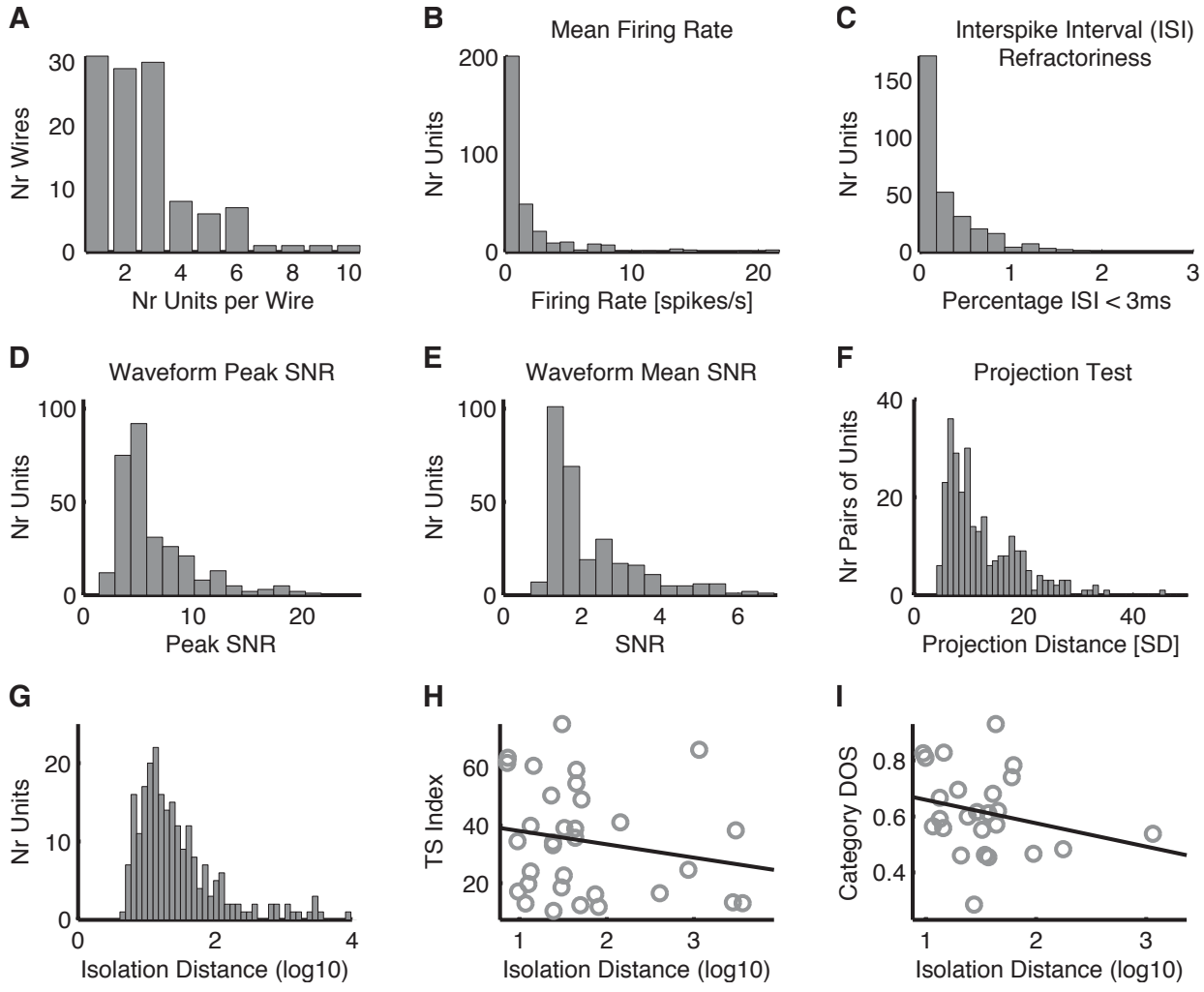

Figure S2. Spike sorting and recording quality assessment, Related to Figure 2. (A) Histogram of the number of units identified on each active wire (only wires with at least one unit identified are counted). The average yield per wire with at least one unit was 2.76±1.79 (mean±SD). **(B)** Histogram of mean firing rates. **(C)** Histogram of proportion of inter-spike intervals (ISIs) which are shorter than 3ms. The large majority of clusters had less than 0.5% of such short ISIs. **(D)** Histogram of the SNR of the mean waveform peak of each unit. **(E)** Histogram of the SNR of the entire waveform of all units. **(F)** Pairwise distance between all possible pairs of units on all wires where more than 1 cluster was isolated. Distances are expressed in units of SD after normalizing the data such that the distribution of waveforms around their mean is equal to 1. **(G)** Isolation distance of all units for which this metric was defined (n=230, median=19.2). **(H)** Absence of correlation between isolation distance and TSI ($r=-0.19$, $P=0.30$). **(I)** Absence of correlation between isolation distance and DOS ($r=-0.25$, $P=0.23$). Each circle represents a TS **(H)** or category **(I)** neuron (category-selective). The black line represents the linear fit.

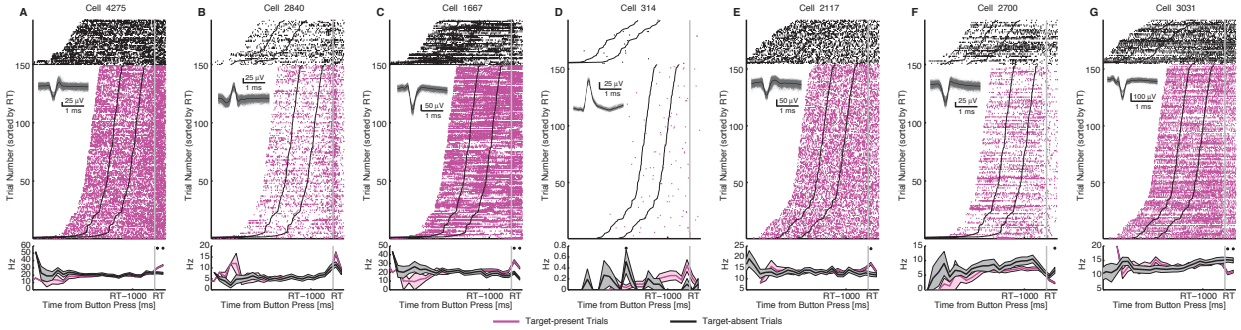

Figure S3. Single-unit examples of target neurons aligned to button press (RT), Related to Figure 2. **(A-E)** Example target neurons with a higher firing rate for target-present trials compared with target-absent trials (selection by two-tailed t-test in a time window of −500 ms to 500 ms around button press (RT): all Ps < 0.05). **(F-G)** Example target neurons with a higher firing rate for target-absent trials compared with target-present trials (all Ps < 0.05). Each raster (upper) and PSTH (lower) is shown with color coding as indicated. Trials are aligned to button presses (gray line) and black lines represent search cue period (fixed 1 second). Trials within each category are sorted according to reaction time. Waveforms for each unit are shown in the raster plot. In the PSTH plot, asterisk indicates a significant difference between the response to target-present trials and target-absent trials in that bin (P < 0.05, two-tailed t-test, Bonferroni-corrected; bin size = 250 ms). Shaded area denotes ±SEM across trials.

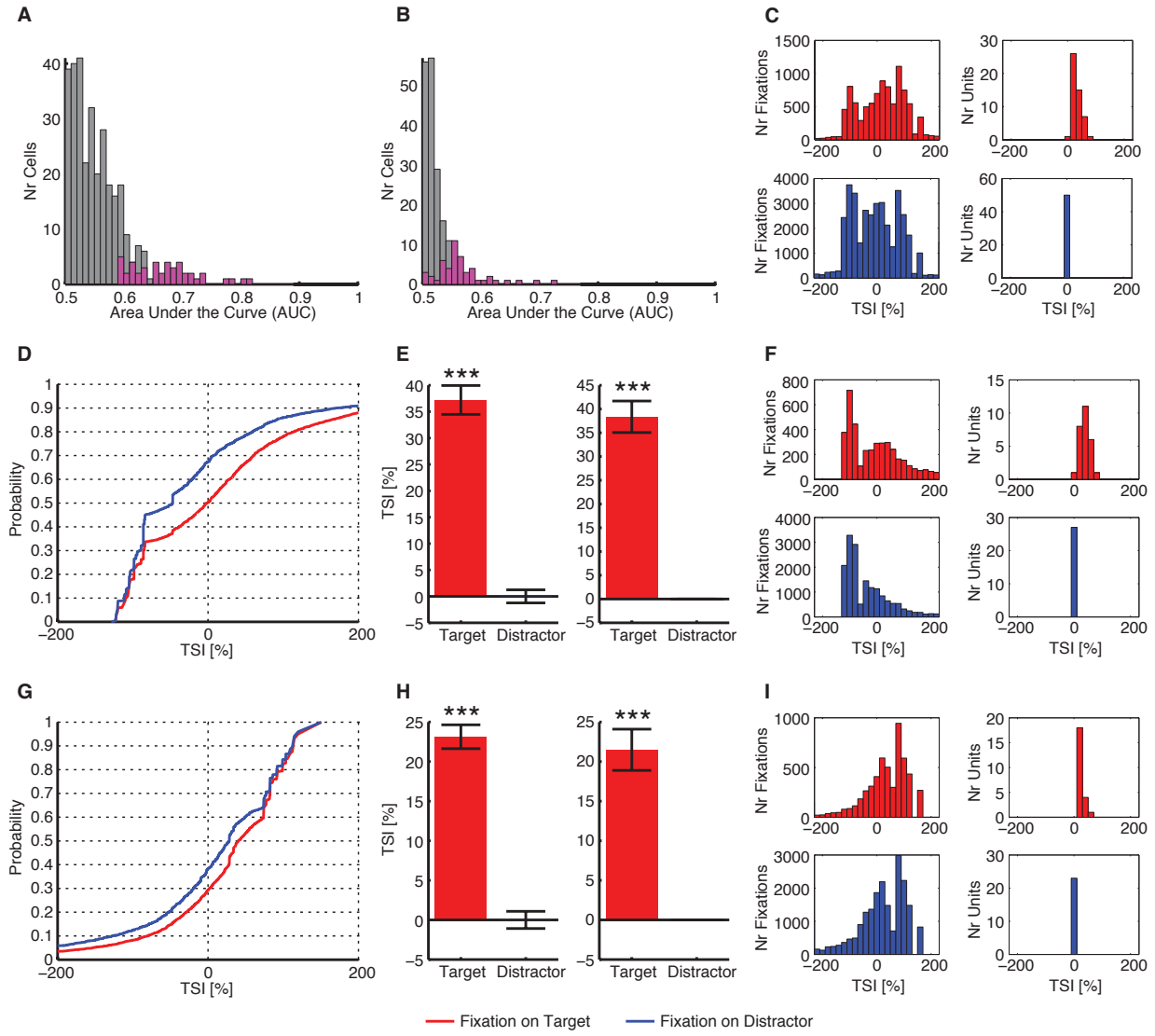

Figure S4. Group results of target neurons, Related to Figure 2. (A) Histogram of AUC values for neurons selected by a significantly different response between target-present and target-absent trials (magenta) and unselected neurons (gray). **(B)** Histogram of AUC values for neurons selected by a significantly different response to fixations on targets vs. distractors (magenta) and unselected neurons (gray). **(C, F, I)** Histogram of the TSI for combined target-preferring and distractor-preferring **(C)**, target-preferring **(F)**, and distractor-preferring **(I)** neurons. TSI was calculated as the baseline-normalized difference in response to fixations on targets compared with fixations on distractors. Top left: TSI for fixations on targets; bottom left: TSI for fixations on distractors; top right: TSI for fixations on targets averaged for each unit; bottom right: TSI for fixations on distractors averaged for each unit. **(D, G)** Cumulative distribution of the TSI for target-preferring **(D)** and distractor-preferring **(G)** neurons. The response was significantly different between fixations on targets and fixations on distractors for either type of neuron (Kolmogorov–Smirnov test, $P < 0.05$ for both comparisons). **(E, H)** Left: Mean TSI across all fixations for target-preferring **(E)** and distractor-preferring **(H)** neurons. Error bar denotes ±SEM across fixations. Right: Mean TSI across all target-preferring **(E)** and distractor-preferring **(H)** neurons. Error bar denotes ±SEM across neurons. Two-tailed one-sample t-tests are indicated by ***: $P < 0.001$.

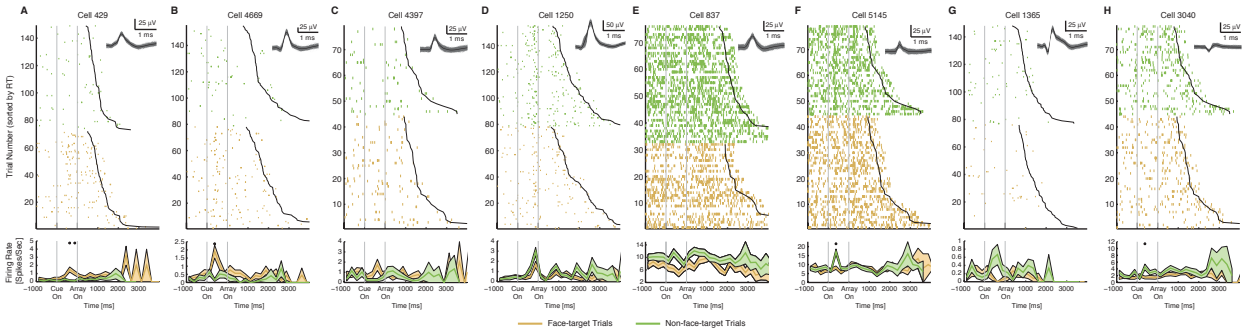

Figure S5. More single-unit examples of neurons showing visual selectivity of faces vs. non-faces during search cue, Related to Figure 3. Legend conventions as in **Figure 3A-E**.

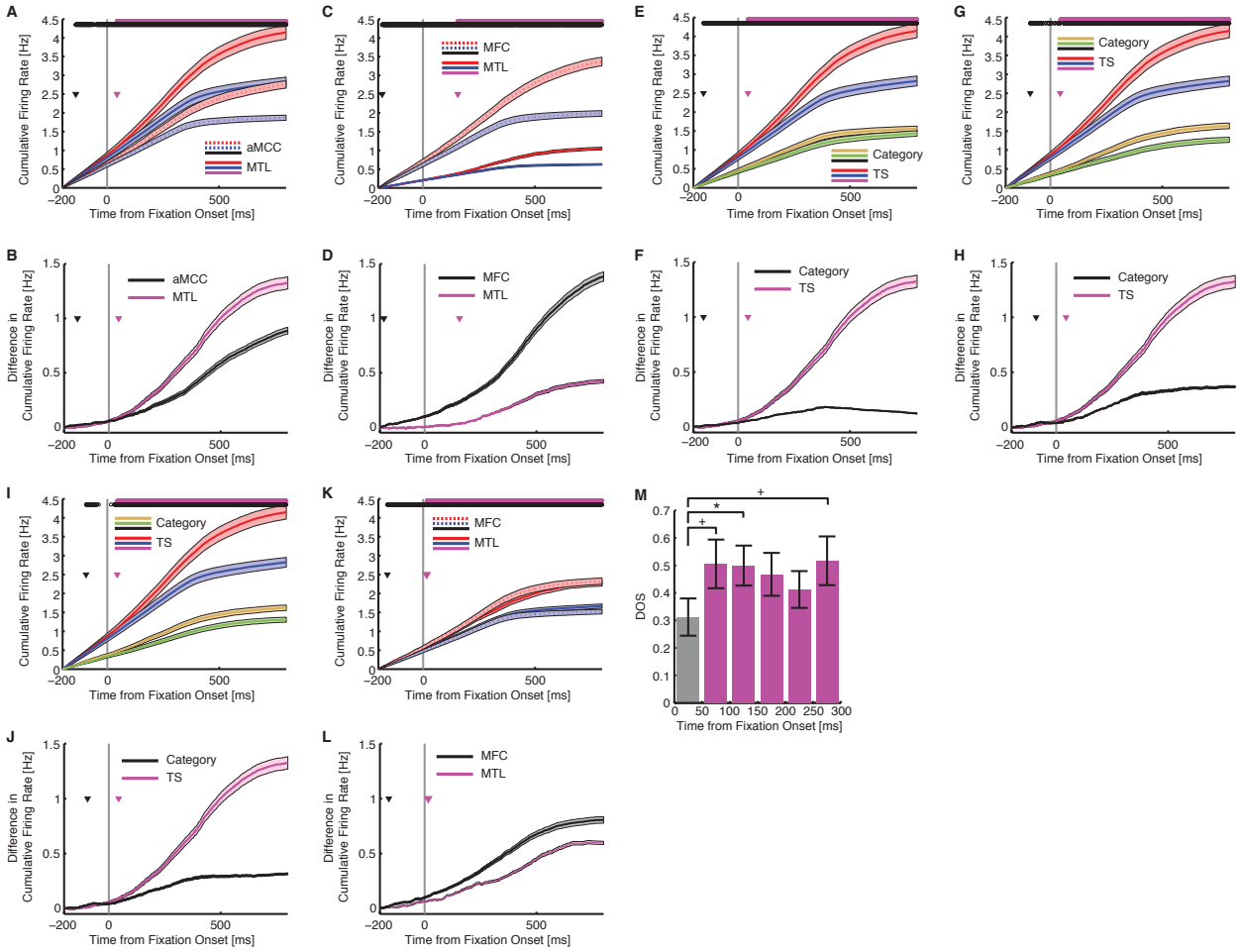

Figure S6. Control results for differential latency analysis, Related to Figure 5. (A-B) Comparison of latency between the MTL and aMCC TS neurons. We recorded 211 neurons from the aMCC and 162 neurons had a firing rate > 0.2Hz. We found 42 TS neurons (25.9%, binomial $P < 10^{-50}$), and 18 increased firing for targets. **(A)** Cumulative firing rate for TS neurons from the aMCC (dotted lines; n = 18 neurons) and MTL (solid lines; n = 27 neurons). Shaded area denotes ±SEM across neurons. Red: fixations on targets. Blue: fixations on distractors. Top bars show clusters of time points with a significant difference (one-tailed pairwise t-test; $P < 0.01$; FDR-corrected; cluster size > 10 time points). Arrows indicate the first time point of the significant cluster (aMCC: −140ms relative to fixation onset; MTL: 44m). Magenta: MTL neurons. Black: aMCC neurons. **(B)** Difference in cumulative firing rate. Shaded area denotes ±SEM across neurons. Arrows indicate the first time point of the significant cluster. Magenta: MTL neurons. Black: aMCC neurons. **(C-D)** Comparison of latency between the MTL (n = 9 neurons) and MFC (n = 24 neurons) TS neurons that were recorded simultaneously. Magenta: MTL. Black: MFC. Note that due to fewer neurons involved, we used a lower threshold to detect significant time points (one-tailed pairwise t-test; $P < 0.05$; FDR-corrected; cluster size > 10 time points). However, we still observed that MFC neurons responded substantially earlier than MTL neurons (MFC: −182ms relative to fixation onset; MTL: 156ms). **(E-F)** Bottom-up category response was faster than top-down TS response (category: −155ms relative to fixation onset; TS: 44ms). Here we selected a population of category neurons whose response differentiated between fixations on faces and non-faces during search (two-tailed two-sample t-test; n = 27; 17 neurons had a greater response for faces and we focused on this subset here). Magenta: TS neurons. Black: category neurons. Brown: fixations on faces. Green: fixations on non-faces. **(G-J)** Comparison with face-selective neurons that were selected during cue presentation. We focused on face-

selective neurons because they had a clear preferred and non-preferred category, and we calculated latency for fixations on targets during search. **(G-H)** Face-selective neurons with faces as the preferred stimulus responded earlier than TS neurons (face-selective: −90ms relative to fixation onset; TS: 44ms). **(I-J)** Combining face-selective neurons with faces as the preferred stimulus and face-selective neurons with non-faces as the preferred stimulus, we found that face-selective neurons encoded preferred stimulus faster than TS neurons (face-selective: −95ms relative to fixation onset; TS: 44ms). **(K-L)** Comparison of latency between the MTL (n = 9 neurons) and MFC (n = 29 neurons) TS neurons in the pop-out task. Magenta: MTL. Black: MFC. **(M)** Temporal evolution of DOS for fixations on targets. Gray: time window before TS neurons became selective. Magenta: time windows after TS neurons became selective. Asterisks in indicate significant difference between DOS values (two-tailed paired t-test): +: $P < 0.1$, and *: $P < 0.05$.

Table S1. List of patients and neurons, Related to STAR Methods.

ID	Age	Sex	Epilepsy diagnosis	Nr Amygdala Neurons					Nr Hippocampus Neurons				
				Total	Left	Right	Targ	Distr	Total	Left	Right	Targ	Distr
C29	19	M	Left temporal neocortical	16	6	0	1	1	8	1	6	3	1
				31	18	5	2	1	33	4	25	12	1
C31	31	M	Left temporal neocortical	0	0	0	0	0	7	1	1	0	0
C32	19	M	Not localized (generalized)	25	0	19	0	0	0	0	0	0	0
C33	44	F	Right temporal	11	0	9	0	3	5	0	4	0	0
C34	70	M	Bilateral temporal	28	10	11	1	1	5	4	0	0	1
				33	14	7	2	0	0	0	0	0	0
C35	63	M	Left temporal neocortical	8	0	7	0	2	2	2	0	1	0
				13	0	11	1	1	5	5	0	2	0
C36	45	M	Right hippocampus	30	22	0	1	2	35	21	0	1	9
C37	33	F	Right hippocampus	22	8	7	0	0	0	0	0	0	0
Sum				217	78	76	8	11	100	38	36	19	12

Patients C29, C34 and C35 performed two sessions (Each row of neurons represent a separate recording session. Each session was recorded on a separate day). Total: all neurons recorded from an area. Left: neurons that were recorded from the left side of an area and had a firing rate greater than 0.2Hz. Right: neurons that were recorded from the right side of an area and had a firing rate greater than 0.2Hz. These neurons were included for further analysis. Targ: target-preferring neurons (neurons that showed significantly greater responses to fixations on targets than distractors). Distr: distractor-preferring neurons (neurons that showed significantly greater responses to fixations on distractors than targets).